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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/429,003	10/29/99	SHARMA	P Q-56359

HM12/0524
SUGHRUE MION ZINN MACPEAK & SEAS PLLC
2100 PENNSYLVANIA AVENUE NW
WASHINGTON DC 20037-3213

EXAMINER	
EINSMANN, J	
ART UNIT	**PAPER NUMBER**
1655	7

DATE MAILED: 05/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/429,003	SHARMA ET AL.	
	Examiner	Art Unit	
	Juliet C. Einsmann	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *01 February 2000 and 29 October 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821-1.825 because CRF is missing. In addition, each time a sequence is recited in the specification it should be followed by a proper sequence identifier (see p. 29-31). Applicant is required to submit a new CRF and an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification and a letter stating that the content of the paper and computer readable copies are the same.

2. The priority document submitted 2/1/2000 has been received and entered into the file (Paper number 4).

3. It is noted that this application is a continuation of PCT/GB98/01261 under USC 120 (as indicated in the first line of the specification and in the declaration), not a 371 application as is indicated on the filing receipt. The examiner expects that this discrepancy will be corrected internally after the mailing of this action, however, applicant may wish to request a corrected filing receipt to confirm that the correction has been made.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 is indefinite because it depends on a later claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 18-25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Wadhwa *et al.* (Molecular Biotechnology, Vol. 6, 1996, p. 213-217).

Wadhwa *et al.* teach a method of obtaining isolated selected cDNA species which comprising:

(a) isolating mRNA from a normal mouse cell line, reverse transcribing the mRNA, amplifying the cDNA, and labeling the resulting cDNA with denaturing loading dye (p. 214);

(b) isolating mRNA from a transformed clone, reverse transcribing the mRNA, amplifying the cDNA, and labeling the resulting cDNA with denaturing loading dye (p. 214);

(c) separating the cDNA species using gel electrophoresis (p. 214)

(d) selecting two or more cDNA species from the separated cDNA species obtained in step (c), which are present at a different level in the normal sample than in the diseased sample (Fig. 1)

(e) isolating and amplifying the resulting selected cDNA species (p. 215); and

(f) immobilizing the resulting isolated selected cDNA species on a Hybond N^+ membrane filter (p. 215).

Wadhwa *et al.* further teach that 16 primer pairs were used to amplify the cDNA's, and that for each of these primer pairs 3-5 differentially expressed bands were seen in either of the two samples (p. 215), resulting in a total of 48-80 differentially expressed bands, and that all of theses bands were isolated from the gel (p. 215).

The method taught by Wadhwa *et al.* clearly anticipates the claimed methods.

8. Claims 18, 21-23, 25-26, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Graber *et al.* (Annals of Surgical Oncology, 3(2): 192-197).

Graber *et al.* teach a method of obtaining isolated selected cDNA species which comprising:

(a) isolating mRNA from a normal esophageal mucosa tissue sample, reverse transcribing the mRNA, and amplifying the cDNA (p. 193);

(b) isolating mRNA from a carcinoma of the esophagus sample, reverse transcribing the mRNA, and amplifying the cDNA (p. 193);

(c) separating the cDNA species using gel electrophoresis (p. 193)

(d) selecting two or more cDNA species from the separated cDNA species obtained in step (c), which are present at a different level in the normal sample than in the diseased sample (Fig. 1); and

(e) isolating the resulting selected cDNA species by excision from the gel (p. 194).

The tissue samples were human tissue obtained from The Cooperative Human Tissue Network of the National Disease Research Institute or from patients. With regard to claim 23,

which requires that the cDNA is labeled, Graber *et al.* do not expressly teach this limitation, however, labeling of the cDNA is an inherent property of the autoradiography method that Graber *et al.* use to visualize the bands (p. 193, Fig. 1). Therefore, the methods of Graber *et al.* clearly anticipate the claimed methods.

9. Claims 29-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Pinkel *et al.* (US 5830645).

Pinkel *et al.* teach kits which comprise a solid support having an array of target nucleic acids bound thereto and a container containing nucleic acids representing a normal reference genome or cDNA from a reference cell type (Col. 3. Lines 41-49). Pinkel *et al.* teach that the nucleic acids on the array may be cDNA or RNA (Col. 2, lines 50-54). It is noted that product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps (see MPEP 2113). Furthermore, it is noted that these claims contain a preamble which recites an intended use, however, it is also noted that this use does not confer patentable weight on the product claims since the preamble does not materially change what is present in the kit itself and thus represents an intended use of the kit (see MPEP 2111.02). Therefore, the kits claimed by Pinkel *et al.* anticipate the instantly claimed kits.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wadhwa *et al.* in view of the Stratagene Catalog (1988).

Wadhwa *et al.* teach a method of obtaining isolated selected cDNA species which comprising:

(a) isolating mRNA from a normal mouse cell line, reverse transcribing the mRNA, amplifying the cDNA, and labeling the resulting cDNA with denaturing loading dye (p. 214);

(b) isolating mRNA from a transformed clone, reverse transcribing the mRNA, amplifying the cDNA, and labeling the resulting cDNA with denaturing loading dye (p. 214);

(c) separating the cDNA species using gel electrophoresis (p. 214)

(d) selecting two or more cDNA species from the separated cDNA species obtained in step (c), which are present at a different level in the normal sample than in the diseased sample (Fig. 1)

(e) isolating and amplifying the resulting selected cDNA species (p. 215); and

(f) immobilizing the resulting isolated selected cDNA species on a Hybond N^+ membrane filter (p. 215), thus resulting in a solid support with differentially expressed cDNA's attached.

Furthermore, Wadhwa *et al.* teach methods in which labeled cDNA samples (both normal and transformed samples) are exposed to the immobilized cDNA species to produce a gene transcript pattern.

Wadhwa *et al.* do not teach the packaging of the immobilized cDNA species into a kit, nor do they teach this method as a method for making a kit.

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to used the method disclosed by Wadhwa *et al.* to produce a kit containing the cDNAs

on a solid support and other reagents useful for gene transcript comparisons, such as the a normal and transformed sample as taught by Wadhwa *et al.* to be used in nucleic acid research since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

It is noted that these claims contain a preamble which recites an intended use, however, it is also noted that this use does not confer patentable weight on the product claims since the preamble does not materially change what is present in the kit itself and thus represents an intended use of the kit (see MPEP 2111.02). Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Wadhwa *et al.* in view of the Stratagene catalog.

12. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wadhwa *et al.* in view of the Stratagene Catalog as applied to claims 29-34 above, and further in view of Seilhamer *et al.* (WO 95/20681).

The teachings of Wadhwa *et al.* in view of the Stratagene Catalog is applied to this claim as discussed above.

Wadhwa *et al.* in view of the Stratagene Catalog do not teach a method in which a test sample is compared to a known sample for diagnosis of a disease.

Seilhamer *et al.* teach that a gene transcripts from a biological specimen can be quantified and compared to against the transcripts of a diseased and healthy patients in order to diagnose a

disease (p. 12, lines 5-20). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included such a comparison step in the methods taught by Wadhwa *et al.* in view of the Stratagene catalog in order to have provided a method for the diagnosis of disease since Seilhamer teach that such comparisons are useful for disease diagnosis.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C. Einsmann
Examiner
Art Unit 1655

May 18, 2000